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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PETER KNOX
and
NEIL COOK,
Appellants

Appeal 2008-3380
Application 09/869,630¹
Technology Center 1600

Decided: July 21, 2008

Before ADRIENE LEPIANE HANLON, CAROL A. SPIEGEL, and
RICHARD M. LEOVITZ, *Administrative Patent Judges*.

SPIEGEL, *Administrative Patent Judge*.

DECISION ON APPEAL

¹ Application 09/869,630 ("the 630 application"), filed 21 September 2001, is the national stage entry (35 U.S.C. § 371) of international application PCT/GB99/04395, filed 23 December 1999, which claims benefit under 35 U.S.C. § 119 of United Kingdom application 9828853.3, filed 30 December 1998. The real party in interest is Amersham plc, now GE Healthcare Limited, a part of General Electric (Substitute Appeal Brief in Response to a Non-Compliant Notification, filed 17 May 2007 ("App. Br."), at 1).

I. Statement of the Case

Appellants appeal under 35 U.S.C. § 134 from a final rejection of all the pending claims, claims 1 and 3-10. We have jurisdiction under 35 U.S.C. § 6(b). We AFFIRM.

The subject matter on appeal is directed to a method of using ^{129}Xe NMR (nuclear magnetic resonance) spectroscopy to study biological molecules. Claim 1 is illustrative and reads (App. Br. 11):

1. An *in vitro* method which is a test involving a reaction of one or more biological molecules and which comprises:

labeling one of said biological molecules with hyperpolarized ^{129}Xe , wherein an assay reagent comprises said biological molecules;

conducting said reaction; and

observing a magnetic resonance (NMR) spectrum and/or NMR image of the hyperpolarized ^{129}Xe during the course of said reaction in order to detect a conformational change in the labeled biological molecule.

The Examiner has rejected claims 1 and 3-10 under 35 U.S.C. § 103(a) as unpatentable over Rose² in view of Pines³ (FR⁴ 2; Ans.⁵ 3).

² Rose et al., "Glycoprotein B of the RFHV/KSHV Subfamily of Herpes Viruses," U.S. Patent 6,015,565, issued 18 January 2000, based on application 08/804,439, filed 21 February 1997 ("Rose").

³ Pines et al., "Enhancement of NMR and MRI in the Presence of Hyperpolarized Noble Gases," U.S. Patent 6,426,058 B1, issued 30 July 2002, based on application 08/825,475, filed 28 March 1997 ("Pines").

⁴ Office action mailed 25 July 2006 ("FR").

⁵ Examiner's Answer mailed 17 October 2007 ("Ans.").

The issue is whether Rose and/or Pines teach or suggest all the elements of claims 1 and 3-10. On appeal, Appellants bear the burden of showing reversible error in the Examiner's rejection. Since Appellants have presented the same arguments for claims 1 and 10 and have not separately argued dependent claims 3-9, we decide this appeal on the basis of claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

II. Findings of Fact ("FF")

The following findings of fact, and those set forth in the Discussion, are supported by a preponderance of the evidence of record.

A. Appellants' application

- [1] According to the 630 specification, all macromolecules have a number of discrete hydrophobic and hydrophilic sites (Spec. 1:24).
- [2] Xenon (Xe) is said to label a macromolecule, such as a protein, by weakly binding to specific hydrophobic sites on the surface of or within a cavity of the macromolecule (Spec. 1: 24-27).
- [3] Hyperpolarized xenon is said to have increased NMR sensitivity compared to non-hyperpolarized xenon (Spec. 1:29-30).
- [4] The 630 specification describes

an *in vitro* method which comprises labelling a biological molecule with hyperpolarised xenon, and observing a magnetic resonance spectrum and/or image of the hyperpolarised xenon in the environment of the biological molecule....Any conformational change of the biological molecule...will cause an alteration in the xenon NMR spectrum. Each hydrophobic site in the biological molecule may give rise to a specific and characteristic NMR shift. (Spec. 2:5-13.)

B. Rose

- [5] Rose is directed to polynucleotides, polypeptides, and antibodies derived from or reactive with the products of genes encoding glycoprotein B from a subfamily of herpes viruses (Rose 5:8-12).
- [6] In one embodiment, glycoprotein B polypeptides may be used to detect or assess the status of a herpes virus infection in an individual (Rose 47:16-18).
- [7] For example, the polypeptide or a fragment thereof may be used as a reagent in an immunoassay to detect the presence of glycoprotein B antibodies that may be present in an individual with current or past herpes virus exposure (Rose 47:19-24).
- [8] In another embodiment, a candidate pharmaceutical agent is mixed with a glycoprotein B polypeptide. Candidate pharmaceutical agents that bind to an active site of the glycoprotein B polypeptide would be expected to interfere with glycoprotein B, and hence the herpes virus, activity. (Rose 49:19-25.)
- [9] "Binding of the candidate to the Glycoprotein B may...be observed as a conformational change, detected...by...nuclear magnetic resonance...." (Rose 49:32-35).

C. Pines

- [10] Pines discloses using hyperpolarized noble gases, preferably ^{129}Xe , to enhance and improve NMR and MRI (Pines 1:10-15; 7:53-64; 9:8-10).
- [11] According to Pines, its methods can be used to analyze the structure, chemistry, spatial relationships, etc. of samples, including

polypeptides, proteins, oligonucleotides, antibodies, and glycoproteins (Pines 12:6-26).

III. Examiner's Findings and Conclusion

The Examiner found that as to claims 1 and 10, "Rose disclose[s] the invention substantially as claimed, ... [but] does not explicitly disclose labeling the biological molecule [sic] with hyperpolarized ^{129}Xe to enhance NMR detection" (Ans. 3) as required by claim 1. The Examiner found that Pines discloses this limitation (Ans. 3). The Examiner concluded that it would have been obvious to detect binding or conformational change using NMR as taught by Rose using hyperpolarized ^{129}Xe as taught by Pines in view of Pines' teaching that "hyperpolarized ^{129}Xe will enhance the magnetic resonance signal, as would be desirable for obtaining more accurate results" (Ans. 4).

IV. Appellants' Position

Appellants argue there is no motivation to combine Rose and Pines because neither teaches nor suggests "the NMR spectrum and/or image is observed during the course of the reaction between the candidate and glycoprotein B" (App. Br. 4-5, original emphasis) as is recited in claim 1. Appellants further argue that so much of Rose is directed to polynucleotides, polypeptides, and antibodies derived from or reactive with the products of genes encoding glycoprotein B from a subfamily of herpes viruses and uses thereof, that it is "difficult to believe that Rose would even suggest improving its invention by labeling a biological molecule with hyperpolarized ^{129}Xe to enhance NMR detection" (App. Br. 6).

V. Discussion

A. Legal principles

“During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow.” *In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989). “The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed.” *Id.* Furthermore, while claims are read in light of the specification, specification limitations are not read into the claims. *Id.* at 322.

“Section 103 forbids issuance of a patent when the ‘differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which [the] subject matter pertains.’” *KSR Int’l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1734 (2007) (citation omitted). “If a person of ordinary skill in the art can implement a predictable variation, and would see the benefit of doing so, § 103 likely bars its patentability.” *Id.* at 1731. “A person of ordinary skill in the art is also a person of ordinary creativity, not an automaton.” *Id.* at 1742.

B. Analysis

Regarding Appellants' first argument, we agree with the Examiner (Ans. 5-6) that Rose’s teaching that conformational changes can be detected by NMR (FF 9) suggests observing binding reactivity between a candidate pharmaceutical agent and glycoprotein B at least twice during the reaction, i.e., in the presence and absence of added candidate, to determine whether there had been a change in the NMR spectrum. To hold otherwise presumes

that a person having ordinary skill in the art is unknowledgeable and unskilled. *See In re Sovish*, 769 F.2d 738, 743 (Fed. Cir. 1985).

Appellants reply that the NMR taught by Rose and Pines is a standard NMR procedure "observing the molecules in the molecule and not the signal of the hyperpolarized noble gas" (Reply Br.⁶ 4). This argument is not persuasive. Appellants have not explained how the "standard" NMR procedure taught by Rose and Pines differs from determining the NMR spectrum of a reaction mixture changes when a candidate agent is added to the reaction mixture. Further, Appellants have not pointed to evidence of record establishing what a "standard" NMR procedure is, how it differs from the NMR procedure described in the 630 specification, and why the scope of claim 1, as read by one of ordinary skill in the art in light of the 630 specification, would exclude a "standard" NMR procedure. Argument of counsel cannot take the place of evidence lacking in the record. *Meitzner v. Mindick*, 549 F.2d 775, 782 (CCPA 1977); *see also In re Pearson*, 494 F.2d 1399, 1405 (CCPA 1974) ("Attorney's argument in a brief cannot take the place of evidence."). Therefore, this argument is not persuasive.

Regarding Appellants' second argument, we again agree with the Examiner (Ans. 7-10) that the subject matter of claim 1 would have been *prima facie* obvious. Rose expressly suggests using NMR to detect conformational changes due to a candidate agent binding glycoprotein B (FF 8 and 9). We recognize that Rose does not expressly disclose "improving its invention by labeling a biological molecule with hyperpolarized ¹²⁹Xe to enhance NMR detection." *See* App. Br. 6. However, Pines teaches an improved NMR using hyperpolarized ¹²⁹Xe (FF 10). *See In re Keller*, 642

⁶ Reply Brief filed 17 December 2007 ("Reply Br.").

F.2d 413, 426 (CCPA 1981) (where a rejection is based on a combination of references, one cannot show non-obviousness by attacking the references individually).

Based on the teachings of Pines, we find that one of ordinary skill in the art would have expected hyperpolarized ^{129}Xe to improve the candidate pharmaceutical agent screening method of Rose. The Appellants have failed to establish otherwise. Therefore, this argument is not persuasive.

Finally, we note that Appellants have not submitted relevant evidence of nonobviousness to rebut the Examiner's conclusion of *prima facie* obviousness.

Therefore, based on the foregoing, we AFFIRM the rejection of claims 1 and 3-10 under §103(a) as unpatentable over Rose in view of Pines.

VI. Order

Upon consideration of the record, and for the reasons given, it is

ORDERED that the decision of the Examiner rejecting claims 1 and 3-10 under 35 U.S.C. §103(a) as unpatentable over Rose in view of Pines is AFFIRMED; and

FURTHER ORDERED that no time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R.

§ 1.136(a) (2006).

AFFIRMED

qsg

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Application 09/869,630

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